

Experiment Number: K93025

Route: IV

Species/Strain: Rats/F344/N

Toxicokinetics Data Summary

Compound: Tetralin/ Analyte: Tetralin

CAS Number: 119-64-2

Request Date: 7/11/2023

Request Time: 10:03:16

Lab: Battelle Northwest

Male

Treatment Group (mg/kg)

2 IV Plasma^{a,b}

20 IV Plasma^{a,b}

	2 IV Plasma ^{a,b}	20 IV Plasma ^{a,b}
C ₀ min _{pred} (ug/mL)	0.745 ± 0.15	1.00 ± 0.20
Alpha (minute ⁻¹)	0.0563 ± 0.0058	0.0464 ± 0.0056
Alpha Half-life (minute)	12.3 ± 1.3	14.9 ± 1.8
Beta (minute ⁻¹)	0.00230 ± 0.00025	0.00249 ± 0.00027
Beta Half-life (minute)	301 ± 32	279 ± 31
Cl (mL*kg ⁻¹)	57.5 ± 5.5	35.9 ± 3.4
V ₁ (mL/kg)	1020 ± 97	775 ± 73
AUC _{0-T} (ug*min*g ⁻¹)	32.8 ± 3.1	525 ± 50
AUC _{inf_pred} (ug*min*g ⁻¹)	39.2 ± 1.8	632 ± 20

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Female

Treatment Group (mg/kg)

2 IV Plasma^{a,b}

20 IV Plasma^{a,b}

	2 IV Plasma ^{a,b}	20 IV Plasma ^{a,b}
C ₀ min _{pred} (ug/mL)	0.665 ± 0.12	1.14 ± 0.15
Alpha (minute ⁻¹)	0.0655 ± 0.0055	0.0550 ± 0.0038
Alpha Half-life (minute)	10.6 ± 0.9	12.6 ± 0.9
Beta (minute ⁻¹)	0.00266 ± 0.00028	0.00247 ± 0.00018
Beta Half-life (minute)	260 ± 27	281 ± 20
Cl (mL*kg ⁻¹)	72.8 ± 6.5	37.6 ± 2.6
V ₁ (mL/kg)	1112 ± 99	684 ± 48
AUC _{0-T} (ug*min*g ⁻¹)	25.9 ± 2.3	501 ± 35
AUC _{inf_pred} (ug*min*g ⁻¹)	32.3 ± 0.7	560 ± 19

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LEGEND

MODELING SOFTWARE

SAS version 8.2 PROC NLIN SAS Institute Inc., Cary, NC

MODELING METHOD & BEST FIT MODEL

^a SAS version 8.2 PROC NLIN, SAS Institute Inc., Cary, NC, bi-exponential elimination model-The data were weighted by $1/(\text{mean blood Tetralin concentration})^2$ when fitting.

EXCEPTIONS

^b Where g for C at 0 minute refers to g tissues and kg for Cl refers to kg body weight, Cl is systemic clearance

ANALYTE

Tetralin

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TK PARAMETERS

C_0min_pred = Fitted plasma concentration at time zero (IV only)

Alpha = Hybrid rate constant of the alpha phase

Alpha Half-life = Half-life for the alpha phase

Beta = Hybrid rate constant of the beta phase

Beta Half-Life = Half-life for the beta phase

Cl = Clearance, includes total clearance

V1 = Volume of distribution of the central compartment, includes Vd and V volume of distribution, Vz apparent volume of distribution NCA,
Vapp apparent volume of distribution for intravenous studies

AUC_0-T = Area under the plasma concentration versus time curve, AUC, from time ti (initial) to tf (final), AUClast

AUCinf_pred = Area under the plasma concentration versus time curve, AUC, extrapolated to time equals infinity

TK PARAMETERS PROTOCOL

ANALYSIS METHOD

Toxicokinetic parameters were determined by fitting the Equation $C(t) = A_0e^{-\alpha t} + B_0e^{-\beta t}$ to the data using a nonlinear least-squares fitting program where $C(t)$ is the blood concentration of Tetralin at any postexposure time (t), α and β are the hybrid rate constants (min^{-1}) obtained from the fit and A_0 and B_0 are the intercepts on the ordinate (concentration) axis of the extrapolated initial and terminal phases, respectively. The elimination half-lives for the initial and terminal phases of the concentration versus time profiles were calculated as $\ln 2/\alpha$ or $\ln 2/\beta$, respectively. The maximum blood concentration (C_0) was assumed to occur at t equals 0 and was calculated as $A_0 + B_0$.

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TK PARAMETERS (cont'd)

TK_INTRAVENTOUS PLASMA

2.0 mg/kg, 20 mg/kg Male and Female

Animals received a single bolus intravenous administration of Tetralin through an indwelling jugular cannula. Three rats/sex/dose were bled at each of 11 time points. Blood samples were analyzed by a GC/MS method with a validated range from approximately 0.0006 to 13 ug Tetralin/g blood. The limit of detection (LOD) and experimental limit of quantitation (ELOQ) were 0.0001 and 0.0006 ug Tetralin/g blood, respectively.